Editorial

Bi-directional Ventricular Tachycardia Revised

The nomenclature of bi-directional ventricular tachycardia (BVT) apparently came from its peculiar ECG morphology showing QRS complexes alternatively changing the frontal axis during ventricular tachycardia. Clinically, BVT was reported as early as 1954 and most often seen in digitalis intoxication. The term BVT was therefore not based on the functional mechanism. However, the molecular basis for two types of inherited ion channel diseases that commonly show BVT has recently been partially elucidated. Accordingly, the concept in regard to BVT may require some reconsideration.

Two other pathological conditions with frequently-observed BVT are Andersen-Tawil syndrome (ATS) and catecholaminergic polymorphic ventricular tachycardia (CPVT). **Figure 1** depicts a 12-leads ECG recorded from a case of genotyped ATS. The patient was initially diagnosed with long QT syndrome since her ECG showed a markedly prolonged QT interval and lacked two other clinical hallmarks of ATS: periodic paralysis and dysmorphic features. Cardiac phenotypes in ATS are characterized by prolongation of QT (or QTU) interval associated with various types of ventricular tachycardias including BVT. It is inherited in an autosomal dominant manner and is defined as a potassium channelopathy since it is caused by mutations on the *KCNJ2* gene which encodes for the protein Kir2.1. This potassium channel carries a background K-current (called I_{K1}) whose main feature is to maintain a deep resting membrane potential. *KCNJ2* mutations found in ATS usually produce loss-of-function effects and thus induce a subtle depolarization of the resting membrane potential, which in turn increases the resting intracellular Ca level via the Na/Ca exchanger.

In contrast, mutations in genes encoding for either the ryanodine receptor (RyR2) or the Ca-binding protein (CASQ2) have been shown to cause another type of familial arrhythmia, CPVT. CPVT patients have no structural heart defects and show exercise/emotion-triggered syncope and/or sudden cardiac death mainly during childhood. Inheritance also follows an autosomal dominant trait. Proteins encoded by RyR2 or CASQ2 are both important players for Ca handling of the sarcoplasmic reticulum (SR). In fact, several RyR2 mutations have been shown to increase SR Ca-release into the cytoplasm.

Finally, now coming back to digitalis intoxications, the drug is well known to inhibit membrane Na/K-ATPase and eventually increases intracellular Ca concentration via the Na/Ca exchanger. Therefore, increase in intracellular Ca level turns up to be a common feature among these three distinct diseases. Although a precise mechanism underlying this bizarre form of ventricular tachycardia remains unknown, there may be alternative oscillation in cytosolic Ca concentrations in the presence of severe functional failure of Kir2.1, SR Ca-handling, Na/K-ATPase or Na/Ca exchanger, which may in turn affect the

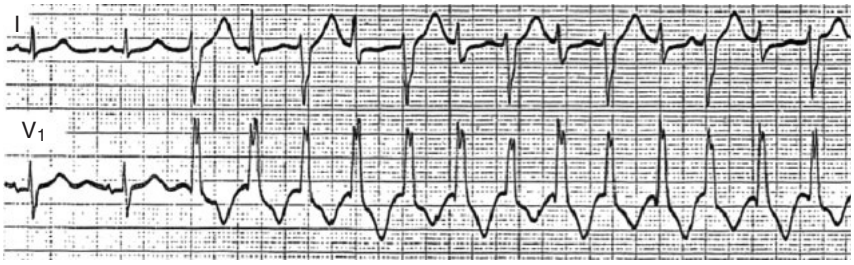

Figure 1 By courtesy of Dr. I Niimura, Yokohama.

morphological ECG features. A computer simulation including intracellular Ca concentrations may offer a clue to answer the mechanistic question in regard to this still-unsolved type of arrhythmia, BVT.

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